IN THE CLAIMS

1. (Original) A pharmaceutical composition comprising a therapeutically active antisense oligonucleotide construct which (i) comprises at least one locked nucleic acid unit selected from the group consisting of amino-LNA and thio-LNA and derivatives thereof; or (ii) comprises at least two consecutively located locked nucleotide units of which at least one is selected from the group consisting of alpha-L-oxy-LNA and derivatives thereof.

2. (Currently Amended) A pharmaceutical composition according to claim 1, in which the antisense oligonucleotide construct comprises two adjacently located nucleotide sequences A and B, where

A represents a sequence of nucleotide units comprising (i) at least one locked nucleotide unit selected from the group consisting of thio-LNA, amino-LNA (both in either alpha-L or beta-D configuration) and derivatives thereof, or (ii) at least two consecutively located locked nucleotide units of which at least one is selected from the group consisting of alpha-L-oxy-LNA and derivatives thereof; and

B represents one nucleotide unit or a sequence of nucleotide units, with the proviso that at least one nucleotide unit in B has a 2'-deoxy-~~erythro~~-pentofuranosyl sugar moiety or a ribo-pentofuranosyl sugar moiety.

3. (Currently Amended) A pharmaceutical composition according to claim 2, in which sequence A additionally comprises at least one further locked nucleotide unit ~~(such as 2, 3, 4 or 5 units), preferably selected independently from the group consisting of amino-LNA, thio-LNA (both in either alpha-L or beta-D configuration), alpha-L-oxy-LNA and derivatives thereof~~.

4. (Currently Amended) A pharmaceutical composition according to ~~any of~~ claims 1~~-2~~, comprising an oligonucleotide construct which contains three adjacently located nucleotide sequences, A, B and C, in the following order (5' to 3'):

A-B-C or C-B-A,

in which

A represents a sequence comprising at least two consecutively located locked nucleotide units, at least one of which is an alpha-L-oxy-LNA unit, and which sequence optionally contains one or more ~~(such as 2, 3, 4 or 5)~~ non-locked nucleotide units ~~(such as deoxyribonucleotide units, ribonucleotide units or derivatives thereof)~~ and/or optionally contains one or more ~~(such as 2, 3, 4 or 5)~~ locked nucleotide units~~, such as a unit selected from the group consisting of oxy-LNA, thio-LNA, amino-LNA (all in either alpha-L or beta-D configuration) and derivatives thereof~~;

B represents one nucleotide unit or a sequence of nucleotide units, with the proviso that at least one nucleotide unit in B has a 2'-deoxy-~~erythro~~-pentofuranosyl sugar moiety or a ribo-pentofuranosyl moiety; and

C represents a sequence comprising at least two consecutively located locked nucleotide units, at least one of which is an alpha-L-oxy-LNA unit, and which sequence optionally contains one or more ~~(such as 2, 3, 4 or 5)~~ non-locked nucleotide units ~~(such as deoxyribonucleotide units, ribonucleotide units or derivatives thereof)~~ and/or optionally contains one or more ~~(such as 2, 3, 4 or 5)~~ locked nucleotide units~~, such as a unit selected from the group consisting of oxy-LNA, thio-LNA, amino-LNA (all in either alpha-L or beta-D configuration) and derivatives thereof~~.

5. (Currently Amended) A pharmaceutical composition according to ~~any of~~ claims 2~~-4~~, in which B represents a sequence of nucleotide units that makes the construct able to recruit RNase H when hybridised to a target nucleic acid.

6. (Currently Amended) A pharmaceutical composition according to ~~any of~~ claims 1~~-5~~, in which the linkages between the nucleotide units in the oligonucleotide construct independently are selected from the group consisting of -O-P(O)$_2$-O-, -O-P(O,S)-O-, -O-P(S)$_2$-O-, -NR^H-P(O)$_2$-O-, -O-P(O,NR^H)-O-, -O-PO(R")-O-, -O-PO(CH$_3$)-O-, and -O-PO(NHR^N)-O-, where R^H is selected form hydrogen and C$_{1-6}$-alkyl, and R" is selected from C$_{1-6}$-alkyl and phenyl.

7. (Currently Amended) A pharmaceutical composition according to ~~any of~~ claims 2~~-6~~, in which the linkages between the nucleotides in sequence B in the oligonucleotide construct comprises at least one linkage which is not a -O-P(O)$_2$-O- linkage~~, such as a phoshorothioate linkage~~.

8. (Currently Amended) A pharmaceutical composition according to ~~any of~~ claims 1~~-7~~, which further comprises a pharmaceutical carrier.

9. (Currently Amended) A pharmaceutical composition according to ~~any of~~ claims 1~~-8~~, which further comprises other antisense compounds, chemotherapeutic compounds, antiinflammatory compounds and/or antiviral compounds.

10. (Original) An oligonucleotide construct which comprises at least one nucleotide sequence comprising one or more nucleotide units selected from the group consisting of amino-LNA, thio-LNA and derivatives thereof;
with the proviso that the following oligonucleotide constructs are excluded:
(i) 5'-d(GTGAVATGC), 5'-d(GVGAVAVGC), 5'-d(GTGAXATGC), 5'-d(GXGAXAXGC), 5'-d(GXGVXVXGC), in which sequences V represents a beta-D-amino-LNA thymine unit, and X represents a beta-D-methylamino-LNA thymine unit; and
(ii) 5'-d(GTGAYATGC), 5'-d(GYGAYAYGC) and 5'-d(GYGYYYYGC) in which sequences Y represents a beta-D-thio-LNA uracil unit.

11. (Currently Amended) An oligonucleotide construct according to claim 10, which comprises two adjacently located nucleotide sequences, A and B, where

A represents a sequence of nucleotide units comprising at least one locked nucleotide unit selected from the group consisting of amino-LNA, thio-LNA ~~(both in either alpha-L or beta-D)~~ configuration, and derivatives thereof; and

B represents one nucleotide unit or a sequence of nucleotide units, with the proviso that at least one nucleotide unit in B has a 2'-deoxy-~~erythro~~-pentofuranosyl sugar moiety or a ribo-pentofuranosyl moiety.

12. (Currently Amended) An oligonucleotide construct according to ~~any of~~ claims 10~~-11~~, which comprises two adjacently located nucleotide sequences, A and B, where

A represents a sequence of nucleotide units comprising at least one locked nucleotide unit selected from the group consisting of amino-LNA, thio-LNA and derivatives thereof; and

B represents a sequence of nucleotide units, said sequence contains a subsequence of at least three nucleotide units having 2'-deoxy-~~erythro~~-pentofuranosyl sugar moieties~~, such as 4, 5, 6, 7, 8, 9 or 10 nucleotide units~~, said subsequence optionally being spiked with an other nucleotide~~, preferably an alpha-L-oxy-LNA unit selected from the group consisting of alpha-L-amino-LNA, alpha-L-thio-LNA, alpha-L-oxy-LNA and derivatives thereof~~.

13. (Currently Amended) A construct according to claim 11~~-12~~, comprising the two adjacently sequences in the following order (5' to 3'):

A-B or B-A.

14. (Currently Amended) A construct according to claim 10~~-13~~, which comprises three adjacently located nucleotide sequences in the following order (5' to 3'):

A-B-C,

in which the nucleotide sequences A and B are as defined in ~~any of~~ claims 11~~-13~~, and C represents a sequence of nucleotide units, which comprises at least one locked nucleotide unit selected from the group consisting of amino-LNA, thio-LNA ~~(both in either alpha-L or beta-D configuration)~~ and derivatives thereof.

15. (Currently Amended) A construct according to ~~any of~~ claims 11~~-14~~, which is selected from the group consisting of (in 5' to 3' order):

A-B, B-A and A-B-C, where

A, B, and C have the same meaning as defined in claims 11~~-14~~, and where

A has a length of 2-10 ~~(preferably 2-8)~~ nucleotide units;

B has a length of 1-10 ~~(preferably 5-8)~~ nucleotide units;

C (if present) has a length of 2-10 ~~(preferably 2-8)~~ nucleotide units; and the overall length of the construct is 6-30 ~~(preferably 10-20, more preferably 12-18)~~ nucleotide units.

16. (Currently Amended) A construct according to ~~any of~~ claims 11~~-15~~, in which A represents a sequence of nucleotide units comprising at least two consecutively located locked nucleotide units ~~(such as 3, 4, 5, 6, 7, 8, 9 or 10 units)~~, at least one of said locked nucleotide units being selected from the group consisting of amino-LNA, thio-LNA and derivatives thereof.

17. (Currently Amended) A construct according to ~~any of~~ claims 11~~-16~~, in which C represents a sequence of nucleotide units comprising at least two consecutively located locked nucleotide units ~~(such as 3, 4, 5, 6, 7, 8, 9 or 10 units)~~, at least one of said locked nucleotide units being selected from the group consisting of amino-LNA, thio-LNA and derivatives thereof.

18. (Currently Amended) A construct according to ~~any of~~ claims 11~~-17~~, in which B represents a sequence of least 2 nucleotide units ~~(such as 3, 4, 5, 6, 7, 8, 9 or 10 units)~~, which sequence in addition to the nucleotide unit(s) having 2'-deoxy-~~erythro~~-pentofuranosyl sugar moiety(ies) and/or ribo-pentofuranosyl moiety(ies), comprises nucleotides units which are selected independently from the group consisting of: locked nucleotide units ~~(such as alpha-L-oxy-, -thio-, or -amino- nucleotide units)~~ and derivatives thereof.

19. (Currently Amended) A construct according to ~~any of~~ claims 10~~-18~~, wherein the linkages between the nucleotide units in the oligonucleotide construct independently are selected from the group consisting of -O-P(O)$_2$-O-, -O-P(O,S)-O-, -O-P(S)$_2$-O-, -NR^H-P(O)$_2$-O-, -O-P(O,NR^H)-O-, -O-PO(R")-O-, -O-PO(CH$_3$)-O-, and -O-PO(NHR^N)-O-, where R^H is selected form hydrogen and C$_{1-6}$-alkyl, and R" is selected from C$_{1-6}$-alkyl and phenyl.

20. (Currently Amended) A construct according to ~~any of~~ claims 11~~-19~~, in which the linkages between the nucleotides in sequence B comprises at least one linkage which is not a -O-P(O)$_2$-O- linkage~~, such as a phoshorothioate (-O-P(O,S)-O-) linkage~~.

21. (Currently Amended) An oligonucleotide construct according to ~~any of~~ claims 11~~-20~~, in which

B represents a sequence of nucleotide units that makes the construct able to recruit RNase H when hybridised to a target nucleic acid.

22. (Currently Amended) An oligonucleotide construct which contains three adjacently located nucleotide sequences, A, B and C, in the following order (5' to 3'):

A-B-C or C-B-A,

in which

A represents a sequence comprising at least two consecutively located locked nucleotide units, at

least one of which is an alpha-L-oxy-LNA unit, and which sequence optionally contains one or more ~~(such as 2, 3, 4 or 5)~~ non-locked nucleotide units ~~(such as deoxyribonucleotide units, ribonucleotide units or derivatives thereof)~~ and/or optionally contains one or more ~~(such as 2, 3, 4 or 5)~~ locked nucleotide units~~, such as a unit selected from the group consisting of oxy-LNA, thio-LNA, amino-LNA (all in either alpha or beta configuration) and derivatives thereof~~;

B represents one nucleotide unit or a sequence of nucleotide units, with the proviso that at least one nucleotide unit in B has a 2'-deoxy-~~erythro~~-pentofuranosyl sugar moiety or a ribo-pentofuranosyl moiety; and

C represents a sequence comprising at least two consecutively located locked nucleotide units, at least one of which is an alpha-L-oxy-LNA unit, and which sequence optionally contains one or more ~~(such as 2, 3, 4 or 5)~~ non-locked nucleotide units ~~(such as deoxyribonucleotide units, ribonucleotide units or derivatives thereof)~~ and/or optionally contains one or more ~~(such as 2, 3, 4 or 5)~~ locked nucleotide units~~, such as a unit selected from the group consisting of oxy-LNA, thio-LNA, amino-LNA (all in either alpha or beta configuration) and derivatives thereof~~.

23. (Original) A construct according to claim 22, in which the three adjacently located nucleotide sequences are in the following order (5' to 3'):

A-B-C.

24. (Currently Amended) A construct according to ~~any of~~ claims 22~~-23~~, which has the formula (in 5' to 3' order):

A-B-C, where

A, B, and C have the same meaning as defined in ~~any of~~ claims 22~~-23~~, and where

A has a length of 2-10 ~~(preferably 2-8)~~ nucleotide units;

B has a length of 1-10 ~~(preferably 5-8)~~ nucleotide units;

C has a length of 2-10 ~~(preferably 2-8)~~ nucleotide units; and the overall lenght of the construct is 8-30 ~~(preferably 10-20)~~ nucleotide units.

25. (Currently Amended) A construct according to ~~any of~~ claims 22~~-24~~, in which A represents a sequence of nucleotide units comprising at least three consecutively located locked nucleotide units, at least one of said locked nucleotide units being selected from the group consisting of alpha-L-oxy-LNA and derivatives thereof.

26. (Currently Amended) A construct according to ~~any of~~ claims 22~~-25~~, in which C represents a sequence of nucleotide units comprising at least three consecutively located locked nucleotide units, at least one of said locked nucleotide units being selected from the group consisting of alpha-L-oxy-LNA and derivatives thereof.

27. (Currently Amended) A construct according to ~~any of~~ claims 22~~-26~~, in which B represents a sequence of least 2 nucleotide units ~~(such as 3, 4, 5, 6, 7, 8, 9 or 10 units)~~, which sequence in addition to the nucleotide unit(s) having 2'-deoxy-~~erythro~~-pentofuranosyl sugar moiety(ies) and/or ribo-pentofuranosyl moiety(ies), comprises nucleotides units which are selected independently from the group consisting of: locked nucleotide units ~~(such as alpha-L-oxy-, -thio-, or -amino- nucleotide units)~~ and derivatives thereof.

28. (Currently Amended) A construct according to ~~any of~~ claims 22~~-27~~, wherein the internucleoside linkages independently are selected from the group consisting of -O-P(O)$_2$-O-, -O-P(O,S)-O-, -O-P(S)$_2$-O-, -NR^H-P(O)$_2$-O-, -O-P(O,NR^H)-O-, -O-PO(R")-O-, -O-PO(CH$_3$)-O-, and -O-PO(NHR^N)-O-, where R^H is selected form hydrogen and C$_{1-6}$-alkyl, and R" is selected from C$_{1-6}$-alkyl and phenyl.

29. (Currently Amended) A construct according to ~~any of~~ claims 22~~-28~~, in which B comprises at least one internucleotide linkage which is not a -O-P(O)$_2$-O- linkage~~, such as a phoshorothioate linkage~~.

30. (Currently Amended) A construct according to ~~any of~~ claims 22~~-29~~, in which B comprises at least one locked nucleotide unit selected from the group consisting of alpha-L-oxy-LNA and derivatives thereof.

31. (Currently Amended) A construct according to ~~any of~~ claims 22~~-30~~, in which A and C comprises at least one alpha-L-oxy-LNA or alpha-L-thio-LNA unit located adjacent to B.

32. (Currently Amended) An oligonucleotide which has the formula (in 5' to 3' order):
A-B-C-D, in which
A represents a sequence of locked nucleotide units;
B represents a sequence of non-locked nucleotide units~~, preferably at least one unit has a 2'-deoxy pentofuranose sugar moiety~~, in which sequence 1 or 2 nucleotide units optionally are substituted with locked nucleotide units~~, preferably alpha-L-oxy-LNA~~;
C represents a sequence of locked nucleotide units; and
D represents a non-locked nucleotide unit or a sequence of non-locked nucleotide units.

33. (Currently Amended) A construct according to ~~any of~~ claims 32, which has the formula (in 5' to 3' order):
A-B-C-D, where
A, B, and C have the same meaning as defined in claim 32, and where
A has a length of 2-6 ~~(preferably 3-5)~~ nucleotide units;
B has a lenght of 4-12 ~~(preferably 6-10)~~ nucleotide units;
C has a length of 1-5 ~~(preferably 2-4)~~ nucleotide units;
D has a lenght of 1-3 ~~(preferably 1-2)~~ nucleotide units; and the overall length of the construct is 8-26 ~~(preferably 12-21)~~ nucleotide units.

34. (Currently Amended) A construct according to ~~any of~~ claims 32~~-33~~, in which

A has a length of 4 nucleotide units;

B has a length of 7-9~~, preferably 8,~~ nucleotide units;

C has a length of 3 nucleotide units;

D has a length of 1 nucleotide unit; and the overall length of the construct is 15-17 ~~(preferably 16)~~ nucleotide units.

35. (Currently Amended) A construct according to ~~any of~~ claims 32~~-34~~, in which the locked nucleotide units in A and C are beta-D-oxy-LNA units.

36. (Currently Amended) A construct according to ~~any of~~ claims 32~~-35~~, wherein the internucleoside linkages independently are selected from the group consisting of -O-P(O)$_2$-O-, -O-P(O,S)-O-, -O-P(S)$_2$-O-, -NR^H-P(O)$_2$-O-, -O-P(O,NR^H)-O-, -O-PO(R")-O-, -O-PO(CH$_3$)-O-, and -O-PO(NHR^N)-O-, where R^H is selected form hydrogen and C$_{1-6}$-alkyl, and R" is selected from C$_{1-6}$-alkyl and phenyl.

37. (Currently Amended) A construct according to ~~any of~~ claims 32~~-36~~, in which B comprises at least one internucleotide linkage which is not a -O-P(O)$_2$-O- linkage~~, such as a phoshorothioate linkage~~.

38. (Currently Amended) An oligonucleotide construct according to ~~any of~~ claims 32~~-37~~, in which

B represents a sequence of nucleotide units that makes the construct able to recruit RNase H when hybridised to a target nucleic acid.

39. (Currently Amended) An oligonucleotide construct which comprises at least one locked nucleotide unit selected from the group consisting of amino-LNA, thio-LNA ~~(both in either alpha-L or beta-D configuration)~~, alpha-L-oxy-LNA, and derivatives thereof;
wherein at least one of the linkages between the nucleotide units is selected from the group consisting of -O-P(O,S)-O-, -O-P(S)$_2$-O-, -NR^H-P(O)$_2$-O-, -O-P(O,NR^H)-O-, -O-PO(R")-O-, -O-PO(CH$_3$)-O-, and -O-PO(NHR^N)-O-, where R^H is selected form hydrogen and C$_{1-6}$-alkyl, and R" is selected from C$_{1-6}$-alkyl and phenyl.

40. (Currently Amended) A construct according to ~~any of~~ claims 39, which comprises at least one phoshorothioate internucleoside linkage.

41. (Currently Amended) A construct according to ~~any of~~ claims 39~~-40~~, which comprises a subsequence of nucleotide units, said nucleotide units having 2'-deoxy-~~erythro~~-pentofuranosyl sugar moieties.

42. (Currently Amended) A method of synthesis of a pharmaceutical composition or constructs according to any one of the claims 1~~-42~~, 10, 22, 32 and 39.